

REMARKS

**Interview summary**

Undersigned counsel for Applicants sincerely thanks Examiner Q. Nguyen for extending the courtesy of a personal interview held on January 3, 2007 at the USPTO (“the Interview”). As noted in the Interview Summary of same date, arguments were presented to overcome the “new matter” and 35 U.S.C. § 103 rejections. While no agreement was reached with respect to the claims, the Examiner agreed to reconsider the rejections in light of the arguments presented below.

**Status of the claims**

Claims 1, 3, 4, 6-9, 12-21 and 23-34 were pending in the instant application. Claim 1 has been amended, but no claims have been added or canceled with this Response. Hence, upon entry of this paper, claims 1, 3, 4, 6-9, 12-21 and 23-34 will remain pending and under active consideration. Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

**Claim rejections under 35 U.S.C. § 112**

Claims 1, 3, 4, 6-9, 12-21 and 23-32 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement of the same statute. Apparently, upon further consideration with quality assurance specialist Christopher Low, the instant Examiner found the phrase “between about 2 hours and about 30 hours postmortem” to lack written support. Judging from the Office Action, the Examiner appears to allege a lack of “literal” support for the quoted phraseology. At least because the M.P.E.P. § 2163.05 III requires that an Examiner “must [also] take into account which ranges one skilled in the art would consider *inherently* supported in the original discussion” when determining whether a numerical range limitation is adequately supported, Applicants respectfully traverse this rejection.

At the Interview, counsel for Applicants introduced the following excerpt from the M.P.E.P.:

In the decision in *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of "25%- 60%" and specific examples of "36%" and "50%." A corresponding new claim limitation to "at least 35%" did not meet the description requirement because the phrase "at least" had no upper limit and caused the claim to read literally on embodiments outside the "25% to 60%" range, *however a limitation to "between 35% and 60%" did meet the description requirement.*" *Id.* (Emphasis added.)

The case at hand similarly described in the original specification a range of "within about 30 hours" postmortem and specific examples of "about 2 hours" and "about 30 hours" postmortem. *See, generally*, Abstract and Section 6.3 of the specification, respectively. Hence, as decided in *Wertheim*, the USPTO must conclude that a limitation of "between about 2 hours and 30 hours postmortem" also meets the description requirement.

Upon presentation of this evidence during the Interview, the Examiner appeared persuaded and preliminarily indicated that the "new matter" rejection would be withdrawn. However, the Examiner did express concern regarding the interpretation of "about 30 hours." As stated in the Office Action, the Examiner alleged that "about 30 hours" could "encompass a postmortem time beyond 30 hours, for example, 30 hours 5 minutes, 30 hours 15 minutes, or even 31 hours; and the as-filed specification clearly teaches that livers [*sic*, are?] obtained postmortem with a maximum 30 hours postmortem (citation omitted)." Applicants respectfully maintain that one of ordinary skill in the art would readily appreciate the metes and bounds of "about 30 hours," however, in an effort to move this case to allowance, Applicants have amended the claims to recite "30 hours."

Taken together, Applicants respectfully submit that the "new matter" rejection has been overcome and respectfully request that the Examiner withdraw same.

### **Claim rejections under 35 U.S.C. § 103**

Claims 1, 3, 4, 6-9, 12-21 and 23-34 stand rejected as allegedly being unpatentable over PCT Application No. WO 95/13697 to Reid *et al.* ("Reid") in view of U.S. Patent No. 6,129,911

to Faris (“Faris”) and newly a cited reference, U.S. Patent No. 5,843,024 to Brasile (“Brasile”) for the reasons of records. Applicants traverse this rejection and discuss each basis for rejection, in turn, below.

All of the elements of the claimed invention are not taught.

In order to establish a *prima facie* case of obviousness, the Office must preliminarily establish that each and every claimed limitation may be found in the prior art. Applicants respectfully submit that the Examiner has failed to meet this threshold requirement. No reference in the art teaches or suggests a method of processing a non-fetal donor liver tissue or procuring liver progenitor cells from a liver tissue obtained between *about 2 hours and 30 hours postmortem*. At least with respect to the primary reference, the Examiner concedes this fact. Office Action, page 6, para. 1. As will be next expounded, neither Faris nor Brasile cure this deficiency.

The Examiner cites Faris for the proposition that liver stem cells can be isolated from deceased donors, including cadavers. Column 5, lines 3-25. But even if this teaching is taken at “face value,” Faris nowhere teaches or suggests that liver progenitor cells can be isolated from liver tissue obtained between “about 2 hours and 30 hours postmortem,” as claimed. In fact, the method for isolating progenitors actually disclosed by Faris, at column 6, lines 5-23, provides that the isolation process, albeit with rats, begins immediately following anesthetization of the donor. There is no indication in Faris that the human liver tissue was isolated any different time, let alone between “about 2 hours and 30 hours postmortem.”

Brasile does not cure the deficiencies of either Reid or Faris. Brasile “admits” that “using organs from heart beating cadavers, the immediate non function rate is estimated to be 25%; and within just 30 minutes of ischemia, the immediate nonfunction rate is increased to about 60%.” Col. 2, lines 27-30. Brasile suggests that flushing and perfusion of livers with a “resuscitation solution” can be used “to overcome the effects of warm ischemia in liver deprived of blood flow, and support a repair process to the degree that impairment of liver function can be reversed.”

Col. 17, lines 57-61. However, Brasile provides no evidence of repair or function. Example 9, wherein liver resuscitation is taught, is a merely a prophetic example. The lack of evidence is significant here. For instance, do the resuscitated livers have regenerative capacity? Indeed, even assuming, *arguendo*, that Brasile's resuscitation solution can "reverse" impairment of liver *function*, there is no teaching or suggestion that *progenitors* can be isolated from these "impairment-reversed" livers, let alone between about "2 hours and 30 hours postmortem." As will be discussed below, prior to the instant disclosure, stem cells had been thought to be particularly sensitive to ischemia, and dead cells cannot be resuscitated.

Simply put, the cited references, alone or in combination, fail to teach, at least, the element of processing a non-fetal donor liver tissue or procuring liver progenitor cells from a liver tissue obtained between about 2 hours and about 30 hours postmortem. This fact, alone, undermines a *prima facie* case of obviousness.

There exists no motivation to combine the reference teachings.

The Examiner's allegation that one of ordinary skill in the art would have been motivated to modify the reference teachings rests entirely on an independent and uncorroborated assumption: that if a method of isolation of stem cells from livers *less* than 2 hours postmortem was known (*e.g.*, Reid, Faris) and there was suggestion that livers up to 6 hours postmortem could be resuscitated to revive some liver function (*e.g.*, Brasile), then one of ordinary skill would be motivated to try to isolate stem cells from the resuscitated livers. This is a conclusion without support. In which *reference* does the Examiner find that one of ordinary skill would had the motivation to isolate stem cells from any liver tissue obtained between about 2 hours and about 30 hours postmortem, including resuscitated ones?

When presented with this question during the Interview, the Examiner acknowledged that he had uncovered no such reference. Rather, the Examiner appeared to explain the silence in the art by taking the position that no one in the art isolated liver progenitors from livers greater than 2 hours because no one had the need (presumably because livers less than 2 hours postmortem, at

least non-human livers, are readily available), but that had one of ordinary skill in the art decided to look for liver progenitor cells in livers greater than 2 hours postmortem, she would know that progenitors could have been isolated therefrom. In other words, the Examiner finds “motivation” in the thought that *if* one of ordinary skill had been motivated to try isolating progenitors from livers between about 2 hours and about 30 hours postmortem, one would have found them. Applicant’s respectfully emphasize that this is not the proper standard for determinations of “motivation”; if it were, this level of “motivation” could be found for every invention patented by the Office.

The Examiner’s allegation cannot be sustained in this manner. The *prior art* must suggest the desirability of the claimed invention. *See* subject heading, M.P.E.P. § 2143.01. Here, the Examiner has found motivation in the Applicant’s disclosure, which is the kind of hindsight bias that courts have attempted to eliminate from determinations of patentability. Applicants respect the Examiner’s prerogative to support an obviousness rejection based on common knowledge in the art or “well-known” prior art. M.P.E.P. § 2144.03. However, if it is the Examiner’s contention that it was “well-known” in the art that progenitor cells could have been isolated from livers between about 2 hours and about 30 hours postmortem, Applicant’s respectfully request that the Examiner take official notice of this alleged fact, according to patent examining procedure. *Id.*

There exists no reasonable expectation of success.

Assuming, *arguendo*, that the elements of the current invention could be found in some combination of the referenced documents and there is a motivation to combine those references, there still remains no reasonable expectation of success in combining or modifying same. The Examiner, here again, provides no evidence in support of the conclusion that an ordinarily skilled artisan would have a reasonable expectation of success to carry out the modification in light of the cited teachings and “high level of skills of an ordinary skilled artisan in the relevant art.” Accordingly, Applicants respectfully traverse this conclusion.

For reasons argued above and in the Response dated May 12, 2006, Reid and Faris both teach that procuring progenitor cells from liver tissue must take place “immediately” upon death. Brasile, which is silent with respect to isolating progenitor cells entirely, nonetheless confirms the understanding at the time that a majority of livers become non-functional after just 30 minutes. As the Applicants stated, “while methods of isolating liver precursor cells are known in the art, until the reduction to the practice of the present invention it was not known that progenitor cells can be isolated from what was considered in the prior art as a “useless” organ (citations omitted).”<sup>1</sup> Specification, para. 0010.

Indeed, the isolation of progenitor cells from livers deemed “useless” was “completely unexpected at the time of invention, since all known prior art references regarded ischemically damaged organs as being totally useless for any meaningful purpose.” Specification, para. 0016. The scientific community held this view because it assumed that the liver autolyzes within less than an hour, and that progenitor cells—being particularly sensitive to ischemic damage—would be the first cells to die. The Examiner’s review of the literature to-date confirms this statement and therefore lends convincing weight to Applicants assertion that one skilled in the art would *not* have expected any success in isolating progenitor cells from tissue greater than about 2 hours postmortem.

In sum, Applicants submit respectfully that the rejection of claims 1, 3, 4, 6-9, 12-21 and 23-34 under 35 U.S.C. § 103 has been traversed, and Applicants request respectfully that the rejection of same claims be withdrawn.

#### **Claim rejections under 35 U.S.C. § 101**

Claims 1, 3, 4, 6-9, 12-21 and 23-34 stand provisionally rejected under 35 U.S.C. § 101 for allegedly claiming the same invention of co-pending application no. 10/620,433. Applicants

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<sup>1</sup> Applicants have previously argued that “useless” livers were defined in the context of livers “useless” for transplantation and provided evidence from the Scientific Registry of Transplant Recipients to support the conclusion that livers greater than about 2 hours postmortem would have been “useless.”

respectfully disagree, but in any event, request that the Examiner hold this “provisional” rejection in abeyance until claims are otherwise found allowable in the present case or patented in the co-pending case. *See*, M.P.E.P. § 804 (I)(B).

Claims 1, 2-4, 8-9, 12-21 and 23-34 stand rejected for alleged non-statutory obviousness-type double patenting over claims 1-4 of USP No. 6,069,055 or claims 1-32 of USP No. 6,242,252 in view of Faris and Brasile. The Examiner’s reasons for rejection are set forth on pages 9-12 and essentially reiterate the reasons for rejection under 35 U.S.C. § 103.<sup>2</sup> Applicants respectfully traverse this rejection. At least for the reasons expounded above in rebutting the Examiner’s *prima facie* case for obviousness with the equivalent references, Applicants respectfully submit that the pending claims are not obvious over the cited patents.

Claims 1, 3-4, 8-9, 12-21 and 23-34 stand provisionally rejected for alleged non-statutory obviousness-type double patenting over claims 49, 51-53, 55-58, 60, 62, 63 and 65-69 of co-pending application no. 10/944,919 in view of Faris and Brasile. The Examiner’s reasons for rejection are set forth on pages 12-14 and follow, in substantial part, the reasons for rejection under 35 U.S.C. § 103. Applicants respectfully disagree with this rejection, but in any event, request that the Examiner hold this “provisional” rejection in abeyance until claims are otherwise found allowable in the present case or patented in the co-pending case. *See*, M.P.E.P. § 804 (I)(B).

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<sup>2</sup> The Reid reference, discussed hereinabove, is identical in disclosure to USP Nos. 6,069,005 and 6,242,252.


Applicants believe that the present application is now in condition for allowance and favorable reconsideration of the application, as amended, is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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